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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,615	06/27/2001	Ian Duncan Rubin	013306-5003	8850

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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 11/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,615	RUBIN ET AL.	
	Examiner	Art Unit	
	Michele Flood	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *13-17,19-24,26-28,31 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,18,25,29,30,32 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/04;9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on August 9, 2004. Acknowledgment is made of newly submitted Claims 35-37.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-12, 18, 25, 29, 30, 32 and 34-37 are under examination.

Response to Arguments

Claims 1-12, 18, 25, 29, 30, 32 and 34 as amended and newly submitted Claims 34-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating and/or reducing the risk of development of type II diabetes in a human or other mammal comprising administering to a mammal in need thereof an effective dose of an extract of a plant of the genus *Trichocaulon* or of the genus *Hoodia* and wherein the claim-designated plant extract comprises a disclosed compound of the structural formula (I), does not reasonably provide enablement for preventing type II diabetes in a mammal comprising the administration of the claim-designated plant extracts to a mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Newly applied as necessitated by amendment.

The claims are drawn to a method of treating or preventing Type II diabetes by administering to a human or other mammal in need thereof an effective dosage of an

extract of a plant of the genus *Trichocaulon* or of the genus *Hoodia*, wherein the extract contains one or more steroidal glycosides.

The factors to be considered in determining whether undue experimentation is required are summarized in In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation added to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

While the specification does reasonably demonstrate orally administering effective amounts of an extract of a plant of the genus *Trichocaulon* or of the genus *Hoodia* comprising a disclosed compound of the structural formula (I) to a mammal in need thereof *per se*, the specification does not demonstrate administering the aforementioned composition for preventing Type II diabetes in a mammal in need thereof comprising the administration of an effective amount of the of the claim-designated plant extracts, as broadly claimed. For example, on page 26, lines 8-11, Applicant discloses an active ingredient found in an extract of either *Trichocaulon* or *Hoodia*: "The Applicant has found that at least one purified fraction has good anti-diabetic activity, and the active principle in the fraction was identified by conventional chemical techniques including nuclear magnetic resonance, and was found to be a compound of the structural formula (1) as shown above [referring to compound of the

general formula (1) as set forth on page 2 of the present specification]." On page 25, line 1 to page 26, line 11, Applicant discloses a method of making one fraction having the claim-designated functional effect of anti-diabetic activity encompassing treating *Trichocaulon* or *Hoodia* plant material, namely stems and roots, with solvents, such as methanol/methylene chloride, *etc.* On page 15 of the present specification, lines 2-8, Applicant discloses advantageously administering effective dose amounts of an anti-diabetic agent comprising a compound of formula (1) to mammals to provide treatment of diabetes. With regard to the treatment of diabetes, the Office notes that Applicant discloses administering an effective amount of the aforementioned compound to inbred ZDF/Gmi rats (a recognized animal model for non-insulin dependent diabetes in humans) resulted in a reduction in the blood glucose concentration from the diabetic level to a similar concentration as in lean littermates after 7 days of treatment; and, maintaining normal glycemia in rats until withdrawal of therapy when blood glucose levels increased in a similar manner in treated rats and control rats, on page 36, lines 8-14. Applicant further discloses that the administration of the aforementioned compound to the test model rats provided the beneficial effects for water and food intake reduction, marginally reducing impaired glucose tolerance, and minimal weight gain, as compared to their lean littermates and/or pair-fed controls. While Applicant discloses that the differences between the treated animals and the lean littermate and/or pair-fed control were not significantly different, it is not apparent from Applicant's disclosure how much difference was measured in the responses of the treated and untreated groups since Applicant provides no comparative data. The Office further notes that while Applicant

discloses treatment with the aforementioned compound to ZDF rats at 6 weeks of age (*i.e.,* pre-diabetic ZDF rat model) resulted in maintenance of normal glycemia until withdrawal of therapy, it is not clear from Applicant's disclosure the length of the treatment of the pre-diabetic animal models.

Inventions targeted for therapy in living subjects should provide evidence because of the unpredictability in biological responses to therapeutic treatments. Claims drawn to pharmaceutically acceptable compositions and methods of administering compounds to living subjects which would in effect 'prevent' the condition from happening require supporting evidence which clearly define the ingredients or constituents therein and supporting data because of the unpredictability in biological responses to therapeutic treatments or therapeutic prophylaxis. In order to enable the skilled artisan to practice the invention as claimed, Applicant would have to demonstrate the functional effect and describe the therapeutic effect or prophylactic effect, and describe the effective amounts of each ingredient for the administration of the composition intended for a therapeutic treatment or prophylaxis.

Moreover, the state of the art at the time the invention was filed did not recognize methods for the prevention of Type II diabetes comprising the administration of pharmaceuticals *per se*, as evidenced by Davies M J et al. (Diabetic Medicine (5/2004), 21(5): 403-414. *"Prevention of Type 2 Diabetes Mellitus. A review of the evidence and its application in a UK setting"*). For instance, Davies teaches Type II diabetes as a complex, metabolic, multifactorial disease wherein the evidence for the prevention of diabetes is for interventions that target individuals at highest risk. Davies teaches

lifestyle interventions, *e.g.,* increased physical activity and decreasing body fat stores, thereby decreasing body weight, decrease the progression of impaired glucose tolerance to diabetes. Davies also teaches administering either traditional or newer pharmacological agents may alter glucose tolerance or reduce the risk of the progression of diabetes. However, Davies does not indicate that there are any known methods to prevent Type II diabetes. In fact, Davies suggests that the administration of pharmacological agents purported to "prevent" diabetes warrant further investigation. For instance, on page 408, Column 1, under *"Acarbose",* Davies discloses that the administration of acarbose to humans produced a 25% relative risk reduction in progression to diabetes compared with placebo. Davies further discloses, "When acarbose was stopped, there was an increase in the incidence of diabetes, suggesting that the benefit of acarbose is only present for as long as it is taken." *See* also Sturis, J et al., American J of Physiology (1995), 269(4Pt 1): E786-92. "*Prevention of diabetes does not completely prevent insulin secretion defects in the ZDF rat*", which discloses "Treatment with acarbose before or with pioglitazone after diabetes onset improved but did not normalize glucose levels, and it did not improve entrainment." Like the acarbose study, the administration of the claim-designated plant extract used in the instantly claimed method disclosed by Applicant results in maintenance of normal glycemia until withdrawal of therapy. Yet, Applicant broadly claims that the administration of the claim-designated plant extracts to either humans or mammals is effective in the prevention Type II diabetes. Thus, while Applicant may have reasonably demonstrated that the oral administration of the claim-designated plant extracts comprising the

aforementioned formula (1) to ZDF/Gmi rats reduces water and food intake, and consequently reduces weight, blood glucose concentration and glucose intolerance, there is no guidance in the specification for the prevention of type II in mammals, including humans. Moreover, the instant application does not provide a working example providing data that shows that the composition of the instant claims would indeed prevent or eliminate the claim-designated disease condition, as readily admitted by Applicant. Thus, Applicant has not demonstrated a method for preventing Type II diabetes mammals in need thereof comprising the administration of the claim-designated plant extracts of either T*richocaulon* or *Hoodia*, as broadly claimed, other than the aforementioned and demonstrated treatment of non-insulin dependent type II diabetes comprising the administration of effective amounts of the claim-designated plant extracts comprising formula (1) to a mammal in need thereof.

Accordingly, it would take undue experimentation without a reasonable expectation of success for one skill in the art to prepare a pharmaceutical composition from the claimed ingredients which have the functional effect for preventing and/or treating any and all types of diabetes in any and all mammals, as broadly claimed by Applicant.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele C. Flood

MICHELE FLOOD
PATENT EXAMINER

MCF
October 25, 2004